

ACAAI 2013 Workshop

Insect Allergy Update

Diagnostic Testing  
for Insect Allergy

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Disclosures of Potential Conflicts of Interest:

Speakers Bureau

Genentech / Novartis

Mylan / Dey

Research / Clinical Trials

Genentech / Novartis

Siemens

Consultant

Stallergenes

Sanofi-Aventis

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Learning Objectives

Upon completion of this session, participants should be able to:

1. Recognize the indications for, and interpretation of, diagnostic tests for venom allergy.
2. Describe the advantages and limitations of new diagnostic materials and methods.

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## Diagnostic Tests for Venom – IgE

- Venom-IgE (skin test or serum) is positive in 15%-25% of asymptomatic (history-neg) adults.
- History-pos / IgE-pos patients have no reaction to sting in 30% - 70% of cases.
- Presence of venom-IgE is not necessarily predictive of clinical reactivity or severity.

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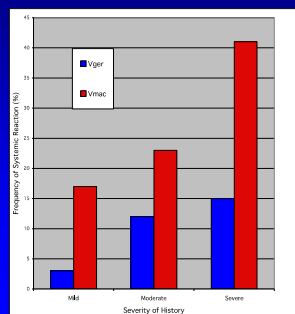
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## Risk of Systemic Reaction Depends on Severity of Previous Reactions and Insect Species

(Golden et al - JACI 2006)




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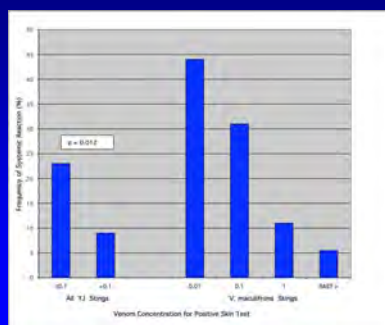
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## Risk of Sting Reaction Related to Venom Skin Test

(Golden et al - JACI 2006)




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### Diagnostic Evaluation of Patients With History of Systemic Reaction to Stings

Golden et al. JACI 2001;107:897.

Skin test positive 68%

ST negative /  
RAST positive 14%

ST neg / RAST neg

sting challenge negative 17%

sting challenge positive 1%

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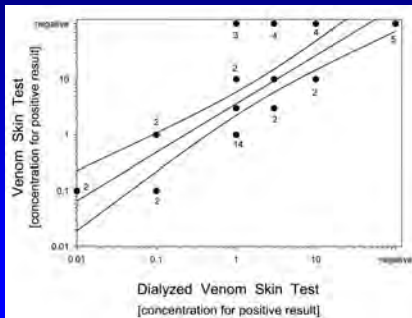
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### Correlation of Dialyzed and Undialyzed Venom Skin Tests

Golden et al JACI 2009;102:47.




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### Natural History of Insect Allergy: Risk Based on Severity of Previous Reactions

Previous Sting Reaction	Chance of Future Systemic Sting Reaction:	
	Any	Severe
Life-threatening	50 - 75%	30%
Moderate Systemic	30 - 50%	10%
Cutaneous Systemic		
– child	1 - 10%	<3%
– adult	10 - 20%	<5%
Large Local	5 - 10%	2%

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Advances in Diagnostic Materials and Methods in Insect Sting Allergy

- Recombinant venom allergens
  - Diagnostic accuracy
  - Cross-reactivity
- Basophil Activation Tests
  - Diagnostic accuracy
  - Predicting systemic reactions

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Recombinant Allergens for Diagnosis of Hymenoptera Venom Allergy

- Muller 2009 – Sensitivity (by ADVIA-Siemens)
  - 96% for rApi m 1; 87% for rVes v 5
- Hofmann 2011 – found 79% for rApi m 1 by ImmunoCAP
- Korosec 2011 – Sensitivity 57% for rApi m 1;
  - 91% for nApi m 1; 100% for HBV
- Mitterman 2010 – “Use of rApi m 1, rApi m 2 and rVes v 5 allows identification of patients with HB and YJ allergy.”
- Sturm 2011 – Using rApi m 1 and rVes v 5 is insufficient, will miss genuine sensitization to other major allergens
- Korosec 2012 – Sensitivity 92% for rVes v 5 or rVes v 1 (84% Vv5, 8% Vv1) ; 100% for YJV

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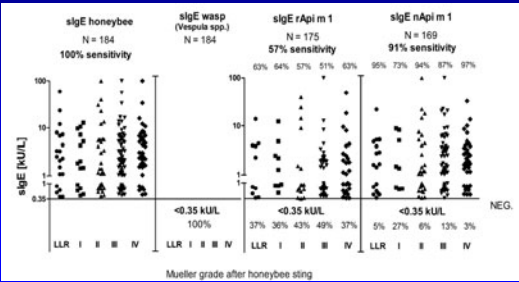
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Low sensitivity of commercial rApi m 1 for diagnosis of HB venom allergy. (Korosec et al. JACI 2011;128:671)



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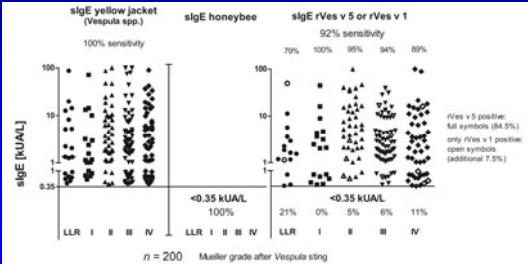
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High sensitivity of CAP-FEIA rVes v 5 and rVes v 1 for diagnosis of *Vespula* venom allergy.  
(Korosec et al. JACI 2012;129: 1406)



Basophil Activation Tests: Reporting Results

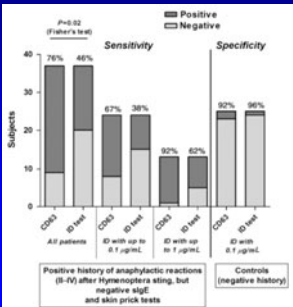
Ratio of “positive” activation to 1.0 vs 0.1 mcg/ml venom (Kosnik 2005)

Proportion of basophils showing increased CD63 expression in response to allergen (cut-off: 15% – Korosec 2009, Kucera 2010; Zitnik 2011; 10% Eberlein 2012; unclear – Peternelj 2008)

CD-sens = 100 / conc for 50% maximal CD63 response (Nopp and Johansson 2009) – Zitnik 2011, Eberlein 2012

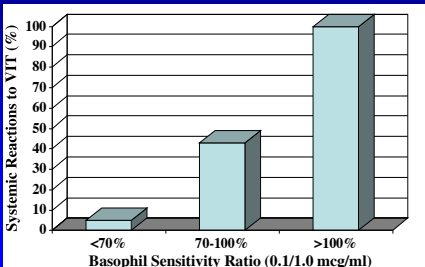
Basophil responsiveness in patients with negative venom-IgE and skin prick tests.

Korosec et al. Clin Exp Allergy 2009;39:1730.



Basophil Sensitivity Ratio Predicts Systemic Reactions to VIT

Kosnik et al. Allergy 2005;60:1401.



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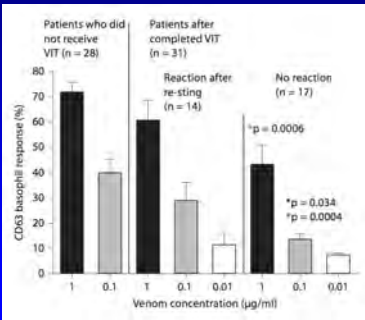
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Basophil sensitivity in patients not responding to VIT.

Petermelj et al. Int Arch Allergy Immunol 2008;146:248.



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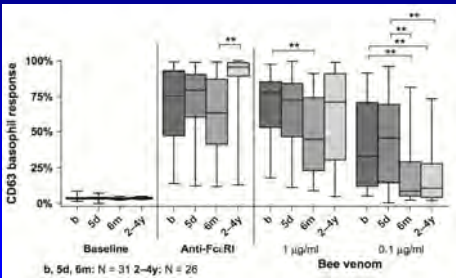
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Monitoring HB VIT in children with the basophil activation test. (Zitnik et al. Ped Allergy Immunol 2012;23:166)



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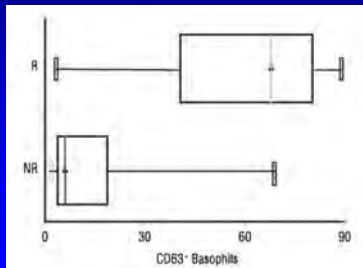
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### Basophil activation predicts sting reaction after VIT

(Kucera et al. J Invest Allergol Clin Immunol 2010;20:110)



### Basophil Activation / Sensitivity Tests in Insect Sting Allergy

Kosnik 2005 – BAT predicts systemic reactions to VIT

Peterneilj 2008 – Basophil CD63 expression higher in patients not responding to VIT

Korosec 2009 – CD63 expression more sensitive (92%) than ID skin tests (62%) in patients with negative serum IgE and negative venom prick tests.

Kucera 2010 – BAT a helpful tool in predicting clinical sensitivity to HB after VIT

Zitnik 2011 – Basophil activation test reflects protective immune response to HB VIT in children.

### Diagnostic Tests for Insect Sting Allergy

Reason for test	Hx	ST	sIgE	BAT	Recomb allergen	RAST inhib	Tryptase baseline
<b>Diagnosis</b>							
No rxn	X						
LLR	X						
Mild SR	X	X	X				
Ana	X	X	X	X	X	X	X
<b>Predict ana (sting / VIT)</b>							
	X			X			X
<b>Cross-reactivity (HB / YJ)</b>							
					X	X	
<b>Stop VIT</b>							
	X			X			X

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Ebo DG, Bridts CH, Hagendorens MM, deClerck LS, Stevens WJ. *The basophil activation test in the diagnosis and follow-up of Hymenoptera venom allergy: An alternative point of view.* J Investig Allergol Clin Immunol 2008;18:482-95.

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Sturm, G.J., et al., *The basophil activation test in the diagnosis of allergy: technical issues and critical factors.* Allergy. 2009. **64**: p. 1319-1326.

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Jakob T, Kohler J, Blank S, et al. *Comparable IgE reactivity to natural and recombinant Api m 1 in cross-reactive carbohydrate determinant-negative patients with bee venom allergy.* J Allergy Clin Immunol 2012;130:276-8.

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